



Burns, Doane, Swecker & Mathis, L.L.P.  
Suite 500  
1737 King Street  
Alexandria, Virginia 22314-2727  
Telephone: +1.703.836.6620  
Group 3 Fax +1.703.836.2021  
Group 4 Fax +1.703.836.0028  
www.burnsdoane.com

## Facsimile Cover

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Date: February 11, 2004

**TO** Examiner Gollamudi Kishore

**Fax Number.** (571) 273-0598

**Company:** USPTO

**Telephone:**

**Your Reference:** 09/976,936

**FROM:** Deborah H. Yellin

**Telephone:** 703.838.6563

**Our Reference:** 033388-371

**Sent By:** Elizabeth K. Stenson

**Number of Pages** 7  
**Including Cover:**

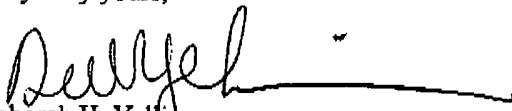
### Message

Dear Examiner Kishore,

In accordance with our phone conversation yesterday, attached please find an Information Disclosure Statement Transmittal Letter, Information Disclosure Statement and Form PTO-1449 in connection with the above-identified application.

Should you have any questions, please do not hesitate to contact us.

Very truly yours,

  
Deborah H. Yellin  
Reg. No. 45,904

Attorney's Docket No. 033388-371**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Patent Application of	)	<b>Mailstop: Reissue</b>
Eric MAYHEW et al.	)	Group Art Unit: 1615
Application No.: 09/976,936	)	Examiner: Gollamudi Kishore, Ph.D.
(Reissue of U.S. Patent No. 5,965,159)	)	Confirmation No.: 1802
Filed: October 11, 2001	)	
For: ETHERLIPID-CONTAINING MULTIPLE	)	
LIPID LIPOSOMES	)	

**FIRST INFORMATION DISCLOSURE STATEMENT**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

In accordance with the duty of disclosure as set forth in 37 C.F.R. § 1.56 and further to 37 C.F.R. § 1.178(b), the accompanying information is being submitted in accordance with 37 C.F.R. §§ 1.97 and 1.98.

All of the listed documents were previously made of record in Application Serial No. 09/017,440 (now U.S. Patent No. 5,965,159), filed February 2, 1998, of which the present application is an application for reissue. In accordance with 37 C.F.R. § 1.98, a copy of each of the listed documents, except those documents which were previously made of record in the prior application, is enclosed.

The documents are being submitted within three (3) months of the filing or entry of the national stage of this application or before the first Office Action on the merits, whichever is later. Since these documents are being filed within the time period set forth in 37 C.F.R. § 1.97(b), no fee or statement is required.

To assist the Examiner, the documents are listed on the attached form PTO-1449. It is respectfully requested that an Examiner initialed copy of this form be returned to the undersigned.

Respectfully submitted,

BURNS, DOANE, SWECKER &amp; MATHIS, L.L.P.

Date February 11, 2004By: Deborah H. Yellin  
Registration No. 45,904

P.O. Box 1404  
Alexandria, Virginia 22313-1404  
(703) 836-6620

(1/04)  
VA 57012 1

Patent  
Attorney Docket No. 033388-371

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of

Eric MAYHEW et al.

Group Art Unit: 1615

Application No.: 09/976,936

Examiner: Gollamudi Kishore, Ph.D.

Filing Date: October 11, 2001

Confirmation No.: 1802

Title: ETHERLIPID-CONTAINING MULTIPLE LIPID LIPOSOMES

FIRST  
INFORMATION DISCLOSURE STATEMENT  
TRANSMITTAL LETTERCommissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

Enclosed is a FIRST Information Disclosure Statement and accompanying form PTO-1449 for the above-identified patent application.

- ☒ No additional fee for submission of an IDS is required.
- ☐ The fee of \$180.00 (1806) as set forth in 37 C.F.R. § 1.17(p) is also enclosed.
- ☐ A statement under 37 C.F.R. § 1.97(e) is also enclosed.
- ☐ A statement under 37 C.F.R. § 1.97(e), and the fee of \$180.00 (1806) as set forth in 37 C.F.R. § 1.17(p) are also enclosed.
- ☐ Charge \_\_\_\_\_ to Deposit Account No. 02-4800 for the fee due.
- ☐ A check in the amount of \_\_\_\_\_ is enclosed for the fee due.


The Director is hereby authorized to charge any appropriate fees under 37 C.F.R. §§ 1.16, 1.17 and 1.21 that may be required by this paper, and to credit any overpayment, to Deposit Account No. 02-4800. This paper is submitted in duplicate.

Respectfully submitted,

BURNS, DOANE, SWECKER &amp; MATHIS, L.L.P.

P.O. Box 1404  
Alexandria, Virginia 22313-1404  
(703) 836-6620Date: February 11, 2004

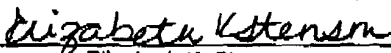
By

  
Deborah H. Yellin  
Registration No. 45,904

I hereby certify that this correspondence is being submitted by facsimile transmission to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, to the following facsimile number:

Facsimile Number: (571) 273-0598

Date of Transmission: February 11, 2004

  
Elizabeth K. Stenson

Typed Name:

BURNS DOANE  
BURNS, DOANE, SWECKER & MATHIS LLP  
INTELLECTUAL PROPERTY LAWFIRST  
INFORMATION DISCLOSURE STATEMENT  
TRANSMITTAL LETTER

(1/04)

Patent  
Attorney Docket No. 033388-371

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of

Eric MAYHEW et al.

Group Art Unit: 1615

Application No.: 09/976,936

Examiner: Gollamudi Kishore, Ph.D.

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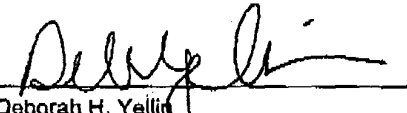
Respectfully submitted,

BURNS, DOANE, SWECKER &amp; MATHIS, L.L.P.

P.O. Box 1404  
Alexandria, Virginia 22313-1404  
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Date: February 11, 2004

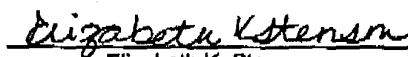
By

  
Deborah H. Yellin  
Registration No. 45,904

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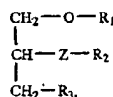
  
Elizabeth K. Stenson  
Typed Name:BURNS DOANE  
BURNS DOANE SWECKER & MATHIS LLP  
INTELLECTUAL PROPERTY LAWFIRST  
INFORMATION DISCLOSURE STATEMENT  
TRANSMITTAL LETTER

(1/04)

- Lewis and McElhane, "The Mesomorphic Phase Behavior of Lipid Bilayers," in *The Structure of Biological Membranes* (P. Yeagle, ed.), CRC Press, Inc. (1992), Boca Raton, Fl., pp. 73-155, at pp. 123-126.
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What is claimed is:

1. A liposome having a lipid bilayer which comprises: (a) a phosphatidylcholine; (b) a sterol; (c) a headgroup-derivatized lipid comprising a phosphatidylethanolamine linked at the ethanolamine group to a dicarboxylic acid; and, (d) an etherlipid having the formula:



wherein  $\text{R}_1$  is  $\text{Y}_1\text{Y}_2$ ,  $\text{Y}_2$  is  $\text{CH}_3$  or  $\text{CO}_2\text{H}$ ,  $\text{Y}_1$  is  $(\text{CH}_2)_{n1}$ ,  $(\text{CH}=\text{CH})_{n2}(\text{CH}_2)_{n3}(\text{CH}=\text{CH})_{n4}(\text{CH}_2)_{n5}(\text{CH}=\text{CH})_{n6}(\text{CH}_2)_{n7}(\text{CH}=\text{CH})_{n8}(\text{CH}_2)_{n9}$ , the sum of  $n1+2n2+n3+2n4+n5+2n6+n7+2n8+n9$  is an integer of from 3 to 23,  $n1$  is zero or an integer of from 1 to 23,  $n3$  is zero or an integer of from 1 to 20,  $n5$  is zero or an integer of from 1 to 17,  $n7$  is zero or an integer of from 1 to 14,  $n9$  is zero or an integer of from 1 to 11, and each of  $n2$ ,  $n4$ ,  $n6$  and  $n8$  is independently zero or 1;

wherein  $\text{Z}$  is oxygen or sulfur and  $\text{R}_2$  is  $\text{CH}_3$ ;

wherein  $\text{R}_3$  is  $-\text{O}-\text{P}(\text{O})_2-\text{O}-\text{CH}_2\text{CH}_2\text{N}(\text{CH}_3)_3$ ;

and wherein the phosphatidylethanolamine-dicarboxylic acid comprises from about 5 mole percent to about 20 mole percent of the lipid bilayer and the etherlipid comprises from greater than about 10 mole percent to less than about 30 mole percent of the lipid bilayer.

2. The liposome of claim 1 which is a unilamellar liposome having a diameter of from greater than about 50 nm to less than about 200 nm.

3. The liposome of claim 1, wherein the phosphatidylcholine is an unsaturated or partially unsaturated phosphatidylcholine.

4. The liposome of claim 3, wherein the phosphatidylcholine is dioleoyl phosphatidylcholine.

5. The liposome of claim 1, wherein the sterol is cholesterol.

6. The liposome of claim 1, wherein the headgroup derivatized lipid comprises a phosphatidylethanolamine selected from the group consisting of dipalmitoyl phosphatidylethanolamine, palmitoyloleoyl phosphatidylethanolamine and dioleoyl phosphatidylethanolamine.

7. The liposome of claim 6, wherein the headgroup derivatized lipid comprises dioleoyl phosphatidylethanolamine.

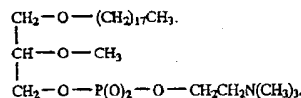
8. The liposome of claim 1, wherein the headgroup-derivatized lipid comprises a dicarboxylic acid selected from the group consisting of glutaric acid, sebacic acid, succinic acid and tartaric acid.

9. The liposome of claim 8, wherein the dicarboxylic acid is glutaric acid.

10. The liposome of claim 1, wherein the headgroup-derivatized lipid comprises dioleoyl phosphatidylethanolamine and glutaric acid.

11. The liposome of claim 1, wherein  $\text{R}_1$  is  $(\text{CH}_2)_{n1}\text{CH}_3$  and  $\text{Z}$  is  $\text{O}$ .

12. The liposome of claim 11, wherein the etherlipid is:



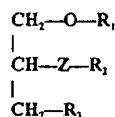
13. The liposome of claim 12, wherein the phosphatidylcholine is dioleoyl phosphatidylethanolamine, the sterol is cholesterol and the headgroup derivatized lipid comprises dioleoyl phosphatidylethanolamine and glutaric acid.

14. The liposome of claim 13, wherein the bilayer comprises about 20 mole percent of the etherlipid, about 10 mole percent of the headgroup-derivatized lipid, about 30 mole percent cholesterol and about 40 mole percent dioleoyl phosphatidylcholine.

15. The liposome of claim 1, comprising an additional bioactive agent.

16. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and the liposome of claim 1.

17. A liposome having a lipid bilayer which comprises: (a) a phosphatidylcholine; (b) a sterol; (c) a headgroup-derivatized lipid comprising a phosphatidylethanolamine linked at the ethanolamine group to a dicarboxylic acid; and, (d) an etherlipid having the formula:



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wherein  $R_1$  is  $Y$ ,  $Y_1$ ,  $Y_2$  is  $CH_2$  or  $CO_2H$ ,  $Y_3$  is  $(CH_2)_n$ ,  $(CH=CH)_m$ ,  $(CH_2)_n$ ,  $(CH=CH)_m$ ,  $(CH_2)_n$ , the sum of  $n_1 + 2n_2 + n_3 + 2n_4 + n_5 + 2n_6 + n_7 + 2n_8 + n_9$  is an integer of from 3 to 23,  $n_1$  is zero or an integer of from 1 to 23,  $n_3$  is zero or an integer of from 1 to 20,  $n_5$  is zero or an integer of from 1 to 17,  $n_7$  is zero or an integer of from 1 to 14,  $n_9$  is zero or an integer of from 1 to 11, and each of  $n_2$ ,  $n_4$ ,  $n_6$  and  $n_8$  is independently zero or 1;

wherein  $Z$  is  $NH$ ,  $C(O)O$ , or  $HNC(O)$ ;

$R_2$  is  $CH_3$ ;

$R_3$  is  $-O-P(O)(-O-CH_2CH_2N(CH_3)_2)$ ; and

wherein the phosphatidylethanolamine-dicarboxylic acid comprises from about 5 mole percent to about 20 mole percent of the lipid bilayer and the etherlipid comprises from greater than about 10 mole percent to less than about 30 mole percent of the lipid bilayer.

18. The liposome of claim 17 which is a unilamellar liposome having a diameter of from greater than about 50 nm to less than about 200 nm.

19. The liposome of claim 17, wherein the phosphatidylcholine is an unsaturated or partially unsaturated phosphatidylcholine.

20. The liposome of claim 19, wherein the phosphatidylcholine is dioleoyl phosphatidylcholine.

21. The liposome of claim 17, wherein the sterol is cholesterol.

22. The liposome of claim 17, wherein the headgroup derivatized lipid comprises a phosphatidylethanolamine selected from the group consisting of dipalmitoyl phosphatidylethanolamine, palmitoyl-oleoyl phosphatidylethanolamine and dioleoyl phosphatidylethanolamine.

23. The liposome of claim 22, wherein the headgroup derivatized lipid comprises dioleoyl phosphatidylethanolamine.

24. The liposome of claim 17, wherein the headgroup-derivatized lipid comprises a dicarboxylic acid selected from the group consisting of glutaric acid, sebacic acid, succinic acid and tartaric acid.

25. The liposome of claim 24, wherein the dicarboxylic acid is glutaric acid.

26. The liposome of claim 17, wherein the headgroup-derivatized lipid comprises dioleoyl phosphatidylethanolamine and glutaric acid.

27. The liposome of claim 17, wherein  $R_1$  is  $(CH_2)_n$ ,  $CH_3$ , and  $Z$  is  $C(O)O$ .

28. The liposome of claim 17, wherein  $R_1$  is  $(CH_2)_n$ ,  $CH_3$ , and  $Z$  is  $NH$ .

29. The liposome of claim 17, wherein  $R_1$  is  $(CH_2)_n$ ,  $CH_3$ , and  $Z$  is  $HNC(O)$ .

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30. The liposome of claim 17, comprising an additional bioactive agent.

31. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and the liposome of claim 17.